REMARKS

Claims 92 and 129 are pending and currently under examination. Claim 92 is rejected under 35 U.S.C. § 112, first paragraph, as lacking adequate written description. Claims 92 and 129 are rejected under 35 U.S.C. § 112, first paragraph, as lacking enablement over the full scope of the claims, and under 35 U.S.C. § 102(b) for anticipation over Tang et al. (WO 01/57190). Each of these rejections is addressed below.

Claim amendments

New claims 132 and 133 have been added. Support for these claims may be found at, e.g., Figure 3a and page 26, lines 28-34, of the specification. No new matter is added by this amendment.

Rejection under 35 U.S.C. § 112, first paragraph, written description

Claim 92 is rejected as lacking adequate written description. The Office states "one skilled in the art cannot reasonably visualize or predict what critical amino acid residues would structurally characterize the genus of polypeptides required to be used in the claimed method. . . the specification fails to describe a single critical amino acid residue required for any definable function in the claimed genus." (Office action, page 3). Applicants disagree.

Applicants would like to draw the Office's attention to page 21 of the application as filed. Here it is described that preferred variants of NsG33 differ from the wild type sequence by one or more conservative and/or semiconservative amino acid substitutions. It is well known to the person skilled in the art that such substitutions typically have minimal influence on the secondary and tertiary structure and the hydrophobic nature of the protein.

The Clustal W alignment in Figure 3a and Figure 3b can be used to predict which amino acid residues can be substituted without substantially affecting the biological activity of the protein. On page 21, lines 16-22, a list defining conservative and semi-conservative substitutions is disclosed. The biological effect of SEQ ID NO:4 is demonstrated in the application as filed peptide variants should contain the biological activity of NsG33. Making substitutions, additions, or deletions to a polypeptide is routine experimentation for the person skilled in the art and does not give rise to any undue burden of experimentation.

The Written Description Training Materials, Example 11, supports the patentability of claim 92. Here, a distinction is made between whether or not a structure and function relationship is present. From the sequence alignment of Figure 3a and 3b, it is evident which amino acids are fully conserved among the three different species (human, mouse and rat). Such fully conserved amino acids would be appreciated by the person skilled in the art to be closely related to the function of the protein, i.e., a structure and function relationship may be derived from figure 3a and 3b. As also stated in the training materials, the skilled person would know that in order to preserve the structure and function of a protein, such fully conserved amino acids can preferably not be altered. If the skilled person nevertheless chooses to make mutations to these fully conserved amino acids, such a mutation can be a so-called conservative mutation as described in the specification (page 21 lines 16-22). Accordingly, the specification identifies the amino acids responsible for the activity of NsG33. The specification also predicts that conservative mutations in these domains will result in a protein having the same activity as NsG33, and the person skilled in the art would expect that many of these conservative substitutions would result in a protein having the required activity. Thus, a correlation exists between the function of the claimed protein and the structure of disclosed fully conserved amino acids shown in Figure 3a and 3b.

As a legal foundation for this rejection, the Office again cites Fiers v. Revel, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) and Univ. of California v. Eli Lilly and Co., 43 USPQ2d 1398 (Fed. Cir. 1997). The Office's reliance on these cases is misplaced as they each presented a very different set of fact from those at hand. In both Fiers and Univ. of California, the claims at dispute were directed to a cDNA corresponding to a previously identified protein (human fibroblast beta-interferon and human insulin, respectively). In neither case did the specification disclose a single cDNA sequence that corresponded to the desired protein. In each case, the court ruled that while it may have been within the skill of one in the art to obtain the claimed cDNA based on the disclosure of the specification, they failed to describe any structural features of the cDNA that would demonstrate possession of the invention.

In contrast to the claims at issue in Fiers and Univ. of California, which were directed to a cDNA sequence that was not disclosed at all in the specification, claim 92 is directed to the use of a genus of polypeptides that are structurally and functionally defined in the specification.

Applicants here have disclosed the polypeptide sequence being claimed and have placed limits on the scope of that sequence. Namely, the polypeptide sequence recited in claim 92 is structurally restricted in two ways: the sequence must be 95% identical to the disclosed SEQ ID NO: 4 and it must contain the recited conserved cysteine residues. Furthermore, the present specification discloses sequences of several NsG33 proteins (i.e. Figure 3 discloses a sequence alignment of NsG33 polypeptides derived from three different species: mouse, rat, and human) and provides significant guidance as to which amino acids may be varied (page 21 lines 16-22). Consequently, the present claims are distinguishable from those confronted in Fiers and Univ. of California, and are well within the scope of patentable subject matter described in Example 11 of the Written Description Training Materials. The rejection of claim 92 for lack of written description should be withdrawn.

Rejections under 35 U.S.C. § 112, first paragraph, enablement

Claims 92 and 129 are rejected for lacking enablement for treatment of patients with Huntington's Disease. The Office states that "treating Huntington's disease encompasses curing this inherited disease, which neither Applicants nor the art reasonably recognize."

The Office's requirement that in order to enable the "treatment of Huntington's Disease" Applicants must further enable "curing" Huntington's disease is not supported by law. As previously stated, in order to satisfy the enablement requirement with respect to the claimed treatment, Applicants are not required to show that every aspect of Huntington's disease is affected by the claimed method. Rather, Applicants can satisfy the enablement requirement through testing in an *in vitro* model that reasonably correlates to the disease to be treated.[1]

On page 50 of the application as filed, treatment of Huntington's Disease according to the present invention is described. It is described that NsG33 is applied to the striatum, preferably the caudate nucleus, in order to protect the neurons from degeneration. In a preferred embodiment, the application should occur before onset of major degenerative changes. Hence, Applicants have not asserted that the administration of NsG33 can cure the disease, but rather that administration of NsG33 is useful to protect the neurons from further degeneration, and thus

[1] See, e.g., M.P.E.P. § 2164.02.

treat Huntington's Disease. In Example 15 of the application as filed, the effect of NsG33 on striatal cultures is described. In Figure 12 it is shown that the addition of conditioned media from ARPE-19 or HEK293T cells transfected with an expression construct containing hNsG33 cDNA increased the percentage of beta-III-tubulin positive neurons significantly in striatal cultures relative to cultures receiving conditioned media from MOCK transfected cultures (see Figure 12, columns "293T-CM33" and "ARPE-CM33"). The increased neuronal number may result from increased differentiation of neuronal progenitor cells present in the cultures and/or a survival effect on the differentiated striatal neurons. This protection of the striatal neurons has subsequently been demonstrated in an in vivo model for Huntington's Disease, as described in the article attached to the last response filed by the applicant (Jørgensen et al., "Lentiviral delivery of Meteorin protects striatal neurons against excitotoxicity and reverses motor deficits in the quinolinic acid rat model," Neurobiology of Disease, in press 2010).

It was well-known in the art at the time of filing that over 90% of the neurons in the striatum are GABAergic neurons (see, e.g., page 391 of Handbook of Psychology, Michael Gallagher, Randy J. Nelson, Irving B. Weiner (2003) and Alexi et al., "Neuroprotective strategies for basal ganglia degeneration: Parkinson's and Huntington's Diseases," 2000, page 436). It was also well-known in the art at the time of filing that medium spiny neurons are GABAergic and represent approximately 90% of the neurons within striatum (see, e.g., page 436, left column and table 6 of Alexi et al. and page 391 of Handbook of Psychology). Hence, by demonstrating protection of striatal neurons as a whole, the inventors also demonstrate protection of GABAergic medium spiny neurons in striatum, i.e., the caudate nucleus and putamen. Consequently, a person skilled in the art would accept that the data presented in the application reasonable correlates with treatment efficacy in Huntington's Disease.

The Office further contends that "Applicant's arguments regarding certain features of their invention are not recited in the rejected claims. Although the claims are interpreted in light of the specification, limitations from the specification… are not read into the claims" (Office action page 5). The features of the invention referenced by the Office are evidence of enablement. In contrast to the Office's contention, it is often necessary and proper that one look

to the specification to support the enablement of the claimed invention.[2] Furthermore, the M.P.E.P. § 2164.08 states:

> One does not look to the claims but to the specification to find out how to practice the claimed invention. *W.L. Gore & Assoc., Inc. v. Garlock, Inc.,* 721 F.2d 1540, 1558, 220 USPQ 303, 316-17 (Fed. Cir. 1983); *In re Johnson*, 558 F.2d 1008, 1017, 194 USPQ 187, 195 (CCPA 1977). In *In re Goffe*, 542 F.2d 564, 567, 191 USPQ 429, 431 (CCPA 1976), the court stated:
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> > [T]o provide effective incentives, claims must adequately protect inventors. To demand that the first to disclose shall limit his claims to what he has found will work or to materials which meet the guidelines specified for "preferred" materials in a process such as the one herein involved would not serve the constitutional purpose of promoting progress in the useful arts.
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> When analyzing the enabled scope of a claim, the teachings of the specification must not be ignored because claims are to be given their broadest reasonable interpretation that is consistent with the specification. "That claims are interpreted in light of the specification does not mean that everything in the specification must be read into the claims." *Raytheon Co. v. Roper Corp.,* 724 F.2d 951, 957, 220 USPQ 592, 597 (Fed. Cir. 1983), *cert. denied,* 469 U.S. 835 (1984). (Underline added).

Therefore, it is improper to require that the exact mechanisms of action and evidence of enablement proffered by Applicants be included as claim limitations. In other words, the present claims recite all of the essential steps for carrying out the methods of the invention, and Applicants' evidence regarding enablement are provided to demonstrate that one skilled in the art would have appreciated that the claimed method was enabled at the time of filing. Consequently, the rejection for lack of enablement should be withdrawn.

Rejections under 35 U.S.C. §102(b)

Claims 92 and 129 are rejected as being anticipated by Tang. The Office asserts that Tang teaches administering the polypeptide of SEQ ID NO: 1401 to treat nervous system disorders. Applicants respectfully disagree.

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2 See, e.g., M.P.E.P. § 2164.01 "Any analysis of whether a particular claim is supported by the disclosure in an application requires a determination of whether that disclosure, when filed, contained sufficient information regarding the subject matter of the claims as to enable one skilled in the pertinent art to make and use the claimed invention."

In the chemical arts, a prior art teaching of genus may only anticipate a species if the species can "at once be envisaged" from the genus. M.P.E.P. § 2131.02. Since, as is explained in more detail below, there is nothing in Tang that would lead one of ordinary skill in the art to at once envisage what is now claimed, the § 102(b) rejection should be withdrawn.

On page 59-61 of Tang, several nervous system disorders are mentioned which may be treated with any of the sequences disclosed in the document. Nervous system disorders are only one of the many categories of disorders and diseases that Tang discloses for treatment with the numerous sequences disclosed in the document. None of the disclosed sequences are preferred over any of the other. Furthermore, nowhere are nervous system disorders preferred over any of the other diseases. Consequently, one skilled in the art would not be able to "at once envisage" the use of a protein of SEQ ID NO: 1401 (a polypeptide selected from a long list of disclosed sequences) for the treatment of Huntington's Disease (a disease selected from a long list of conditions). Tang contains a number of tables (Table 1-5) describing the limited information available regarding the nature and function of the disclosed sequences. Table 5 discloses that SEQ ID NO: 1401 is the full-length peptide sequence and that SEQ ID NO: 417 is the corresponding full-length nucleotide sequence encoding this peptide. Table 4 and 3 fails to identify either SEQ ID NO: 1401 or SEQ ID NO: 417, however table 2 identifies SEQ ID NO 417 as a "novel protein." The only information derivable from Tang is the fact that the authors have isolated a novel protein from human adult brain. Nowhere in Tang is the function of SEQ ID NO: 417 and 1401 disclosed or even hinted at. Accordingly, one skilled in the art would not have envisaged the particular species of the use of a protein with the sequence of SEQ ID NO. 1401 in treatment of Huntington's Disease.

Furthermore, according to M.P.E.P. § 2121, a prior art reference must provide an enabling disclosure of the desired subject matter in order for this prior art to be an anticipating reference. Mere naming or description of the subject matter is insufficient if it cannot be produced without undue experimentation. It would require undue experimentation to arrive at the claimed subject matter based on the complete absence of information regarding the activity of SEQ ID NO:1401 provided by Tang and the multitude of genes and diseases disclosed. Consequently, the rejection for lack of novelty should be withdrawn.

CONCLUSION

Applicant submits that the claims are in condition for allowance and such action is respectfully requested.

If there are any charges or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

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